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DOCKING STUDY OF PIRROLOALLOCOLCHICINOIDS - COLCHICINE-BINDING SITE LIGANDS

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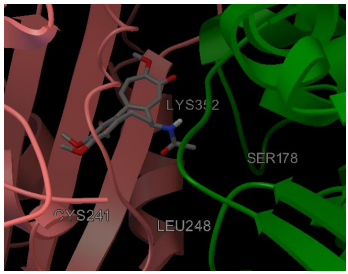
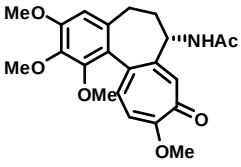
Developing anti-cancer drugs is now one of the most actual problems of medical chemistry and pharmacology. One of the best way to stop the formation of the cancer is blocking the mitosis of the cancer cells.



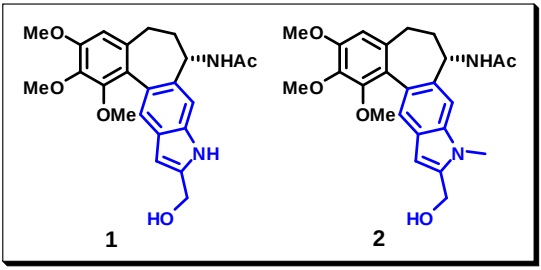
Tubulin is a protein from which microtubules are formed. It is a dimeric protein consisting of two similar subunits - alpha-tubulin and beta-tubulin. It consists three sites which could be bound by antimitotic molecules: tax site, vinca site and colchi site. Taxol, his analogues, and vinca alkaloids are used in clinical practice. But colchicine site agents still have no medical use because of toxicity of colchicine in therapeutical doses.

The colchicine binding site is the region of tubulin molecule which is located on the border of the α- and β-isoforms of this protein. Parametres of the colchicine binding site have been already measured. For achieving better pharmacokinetical parametres, new colchicine analogues - heterocyclic allocolchicinoids - are being synthesized. The topic of our work is the docking study of pirroloallocolchiciniods **1** and **2** which are already synthesized in our group[1]. All calculations are carried out by AutoDock 4.2 (molecular docking).

According to results of docking, molecules **1**, **2** and colchicine have very similar values of binding energy (-8.27 kcal/mol for colchicine, -8.16 kcal/mol for **1** and -7.96 kcal/mol for **2**). But theu have different geometry of binding. **1** has 2 hydrogen bonds with Thr179α (-CH_2OH group and pirrolic hydrogen atom). **2** has 2 hydrogen bonds: with Val238β (-CH_2OH group) and with Ser178α (2-OCH_3 group). [in comparison with colchicine: 1 hydrogen bond: with Val181α (tropolonic C=O group)].



colchicine



1. Shchegravina E.S. et al. *Eur. J. Org. Chem*., 2016: 5620–5623.